The opinion in support of the decision being entered today was <u>not</u> written for publication and is not binding precedent of the Board.

Paper No. 34

#### UNITED STATES PATENT AND TRADEMARK OFFICE

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# BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

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# Ex parte GERRIT VOORDOUW, DONALD W.S. WESTLAKE and PHILLIP M. FEDORAK

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Appeal No. 1995-3965 Application No. 07/719,005

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## ON BRIEF

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Before WILLIAM F. SMITH, SCHEINER, and ADAMS, <u>Administrative Patent Judges</u>.

ADAMS, <u>Administrative Patent Judge</u>.

## **DECISION ON APPEAL**

This is a decision on the appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 1, 3-5 and 7-13, which are all the claims pending in the application.

Claims 1 and 9 are illustrative of the subject matter on appeal and are reproduced below:

- 1. A process for detecting the presence of different selected standard microorganisms in a sample by reverse genome probing, wherein said process comprises the steps of:
  - (A) preparing a master solid surface having affixed thereto isolated spots of genomic deoxyribonucleic acid from each of said different selected standard microorganisms by:
    - obtaining an individual culture of each of said selected standard microorganisms from an environment of interest,
    - (ii) isolating a genomic deoxyribonucleic acid preparation from each of said individual cultures, and
    - (iii) affixing each of said genomic deoxyribonucleic acid preparation from step (Aii) to said master solid surface,
  - (B) preparing a reverse genome probe from said sample by:
    - isolating a total nucleic acid preparation from said sample by:
    - (ii) labeling said total nucleic acid preparation,
  - (C) contacting said master solid surface from step (A) with said reverse genome probe from step (B) under conditions permitting hybridization,
  - (D) washing said master solid surface resulting from step (C) so as to remove non-hybridized reverse genome probe, and
  - (E) detecting hybridized reverse genome probe.
- 9. A master solid surface for use in detecting the presence of different selected standard microorganisms by reverse genome probing, said master solid surface having affixed thereto isolated spots of genomic deoxyribonucleic acid from each of said selected standard microorganisms, wherein said different selected standard microorganisms are isolated from an environment of interest.

The references relied upon by the examiner are:

Hitzman 4,540,052 Sep. 10, 1985

Kimmel, "Selection of Clones from Libraries: Overview," <u>Methods in Eznymology</u>, Vol. 152, pp. 393-399 (1987)

Wang et al. (Wang), "Simultaneous Detection of Both DHBV DNA and DHBV DNA Polymerase by Reverse Spot Hybridization," <u>Chinese J. Microbiol. Immunol.</u>, Vol. 9, No. 4, pp. 261-264 (1989). BIOSIS Abstract only.

## GROUNDS OF REJECTION<sup>1</sup>

Claims 1, 3-5 and 7-13 stand rejected under 35 U.S.C. § 103 as being unpatentable over Wang in view of Hitzman and further in view of Kimmel.

We reverse.

#### DISCUSSION

In reaching our decision in this appeal, we considered appellants' specification and claims, in addition to the respective positions articulated by the appellants and the examiner. We make reference to the examiner's Answer<sup>2</sup>, and the examiner's Supplemental Answer<sup>3</sup> for the examiner's reasoning in support of the rejections. We further reference appellants' Brief<sup>4</sup>, and appellants' Reply Brief<sup>5</sup> for the appellants' arguments in favor of patentability.

#### THE REJECTION UNDER 35 U.S.C. § 103:

Initially, we note that this appeal was remanded to the examiner, at the request of the Office of the Group Director of Technology Center 1600, on April 15, 1998. See Paper No. 32½. However, after reconsideration of the issues on appeal, the examiner returned the application to the Board, where it was returned

<sup>&</sup>lt;sup>1</sup> We note the examiner withdrew (Supplemental Answer, page 1) the rejection of claims 1, 7, 8, 9 and 13 under 35 U.S.C. 102(b) as being unpatentable over the abstract of Wang in view of appellants' amendment received October 7, 1994 (Paper No. 28).

<sup>&</sup>lt;sup>2</sup> Paper No. 27, mailed August 9, 1994.

<sup>&</sup>lt;sup>3</sup> Paper No. 30, mailed November 14, 1994.

<sup>&</sup>lt;sup>4</sup> Paper No. 26, received May 31, 1994.

"to its existing place in the order in which appeals are decided." See Paper No. 33, mailed May 22, 2000.

According to the examiner (Answer, page 5) Wang "teach the detection of hepatitis B virus (HBV) using the 'reverse spot hybridization' which inherently makes use of a 'reverse genome probe." The examiner further explains (<u>id.</u>) that Wang uses Southern blot methodology that includes:

a solid surface such as a nitrocellulose filter or nylon membrane to which DNA is immobilized; a hybridization solution containing a radioactive probe which is incubated with the solid surface under conditions in which the probe hybridizes to the complementary DNA on the solid surface; a wash step in which the unbound probe is washed away; and a detection step in which the position and amount of hybridized probe is measured.

According to the examiner (Answer, page 6) Wang differs from the claimed invention in that Wang does not teach "the use of a plurality of genomic deoxyribonucleic acid spots, [or] the use of a selected standard which is a plurality of microorganisms. In addition, with regard to claims 3, 5 and 11, the examiner finds (<u>id.</u>) that Wang does not teach "an oil field environment ... [or] the use of a sulfate reducing bacterium."

To overcome these deficiencies the examiner relies on Hitzman and Kimmel.

According to the examiner (Answer, page 6) "Hitzman discloses an oil field environment ... and the use of sulfate reducing bacterium." Thus, the examiner finds (id.) that it "would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use the oil field and bacterium of Hitzman in the

<sup>&</sup>lt;sup>5</sup> Paper No. 28, received October 7, 1994.

method of Wang et al. to develop a test for the presence of these bacteria in the oil field." The examiner further finds (Answer, bridging sentence, pages 6-7) that a person of ordinary skill in the art would have been motivated to combine Hitzman with Wang since Hitzman discloses "the presence of microorganisms, particularly sulfate-reducing bacterial, in the flood water causes serious problems of plugging of the oil bearing formation and corrosion of injection and downhole equipment...."

The examiner relies (Answer, page 7) on Kimmel to teach that "[i]ndividual recombinants within libraries can be screened for homology with a nucleic acid sequence ... [i]n addition, populations can be screened as mixtures of recombinants...."

Therefore the examiner concludes (<u>id.</u>) that it "would have been <u>prima facie</u> obvious to one of ordinary skill in the art at the time the invention was made to use the multiple nucleic acid screening of Kimmel with the method of Wang and Hitzman for the expected benefit of constructing a method of detecting multiple nucleic acid sequences in a single experiment."

With regard to Wang and Hitzman, appellants argue (Brief, page 14) that the references are "fundamentally different from the present invention because" neither reference alone or in combination teach or suggest "the use of a reverse gene probe for the detection of more than one microorganism with a single hybridization." Furthermore, while appellants agree (Brief, page 15) that "Kimmel clearly teaches that populations can be screened as mixtures of recombinants", appellants find that "Kimmel does not teach that such screening can be done with a single

hybridization." Therefore, appellants conclude (Answer, page 17) that "[w]hen considering the above-described fundamental difference as a whole, it is crucial to note that Kimmel provides absolutely no suggestion of any technique which would enable the detection of more than one microorganism using a single incubation/hybridization."

In response the examiner argues (Answer, pages 8 and 9) that appellants admit, "in Paper 16, filed May 10, 1993 'that the laboratory procedures required to carry out the reverse hybridization technique are well known and are fully disclosed in Wang et al." We are not persuaded by this argument. While "laboratory procedures" (e.g., Southern Blot procedures) may be well known, it is the claimed invention as a whole that must be considered in an obviousness determination.

See In re Antonie, 559 F.2d 618, 625, 195 USPQ 6, 8 (CCPA 1977). Furthermore, as set forth in In re Nomiya, 509 F.2d 566, 571, 184 USPQ 607, 612 (CCPA 1975) "[t]he court must be ever alert not to read obviousness into an invention on the basis of the applicant's own statements; that is, we must view the prior art without reading into that art appellant's teachings."

The examiner also argues (Answer, pages 9-10) that "Kimmel explicitly teaches the same principle as found in this application, namely, that one could mix probes of different DNA species and use this probe mixture to simultaneously detect complementary DNA of several different species by hybridizing to multiple spots ... with a single hybridization...." Thus the examiner concludes (Answer, bridging sentence, pages 10-11), "[t]aken together with the Wang et al. procedure,

using reverse probes to identify a single organism, these references suggest identifying a plurality of microorganisms using a plurality of probes."

Appellants, however, outline (Reply Brief, pages 5-6) three "differences between the differential scanning technique of the Kimmel review and the process of the present invention...." First, the "dots" of Kimmel's method "are prepared for [sic] the single cDNA, clones or mixture of cDNA clones, and thus represents [sic] only a small portion ... of the genomic DNA of a[n] eukaryotic organism.... In direct contrast [to Kimmel's method] the dots of different selected standards of the present invention are prepared from genomic DNA...." Second, in Kimmel's method "[t]he reverse probe ... is the mRNA of a given eukaryotic organism or the mRNA of a given cell type of a given eukaryotic organism... In direct contrast, the reverse probe of the present invention is prepared from ... all genomic DNA in the sample...." Finally, appellants' argue (Reply Brief, page 6) "the present invention teaches a convenient process for the quick, convenient, initial characterization of different microorganisms in a complex microbial community using a single hybridization. The Kimmel review makes absolutely no such a [sic] teaching."

To this, the examiner finds (Supplemental Answer, page 1) "[t]hese arguments are not persuasive for the reasons of record." We cannot agree. The initial burden of presenting a <u>prima facie</u> case of obviousness rests on the examiner. <u>In re Oetiker</u>, 977 F.2d 1443, 1445, 24 USPQ2d 1443, 1444 (Fed. Cir. 1992). On this record, appellants identify three differences between the claimed invention and the prior art relied upon. These differences highlight Kimmel's failure

to suggest screening a genomic DNA blot with genomic DNA probes. In contrast, the claimed invention <u>requires</u> that a genomic DNA dot blot be probed with genomic DNA. As set forth in <u>Antonie</u> "[j]ust as we look to a chemical and its properties when we examine the obviousness of a composition of matter claim, it is this invention as a whole, and not some part of it, which must be obvious under 35 USC 103. <u>Cf. In</u> <u>re Papesch</u>, 50 CCPA 1276, 315 F.2d 381, 137 USPQ 43 (1963)."

On these facts, we are constrained to reach the conclusion that the examiner failed to provide the evidence necessary to support a <u>prima facie</u> case of obviousness for the invention as a whole. While a person of ordinary skill in the art may possess the requisite knowledge and ability to modify the protocol taught by the combination of Wang, Kimmel, and Hitzman, the modification is not obvious unless the prior art suggested the desirability of the modification. <u>In re Gordon</u>, 733 F.2d 900, 902, 211 USPQ 1125, 1127 (Fed. Cir. 1984). Here, the examiner identifies no such reason to modify the references as applied.

Accordingly, we reverse the rejection of claims 1, 3-5 and 7-13 under 35 U.S.C. § 103 as obvious over Wang in view of Hitzman and further in view of Kimmel.

## OTHER ISSUES

Prior to any further action, the examiner and appellants should consider whether dependent claims 3, 10 and 12 further limit claims 1, 9 and 10 respectively from which they ultimately depend.

## **REVERSED**

William F. Smith Administrative Patent Judge	)
Donald E. Adams	) ) BOARD OF PATENT
Administrative Patent Judge	) ) APPEALS AND
Toni R. Scheiner	) INTERFERENCES
Administrative Patent Judge	)

Application No. 07/719,005

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